



US005585347A

**United States Patent** [19]

Meier et al.

[11] **Patent Number:** 5,585,347[45] **Date of Patent:** Dec. 17, 1996[54] **METHODS FOR THE DETERMINATION AND ADJUSTMENT OF PROLACTIN DAILY RHYTHMS**[75] Inventors: **Albert H. Meier**, Baton Rouge, La.;  
**Anthony H. Cincotta**, Andover, Mass.[73] Assignees: **Ergo Science Incorporated**, Newport, R.I.; **Board of Supervisors of Louisiana State University and Agricultural and Mechanical College**, Baton Rouge, La.[21] Appl. No.: **995,292**[22] Filed: **Dec. 22, 1992****Related U.S. Application Data**

[63] Continuation-in-part of Ser. No. 719,745, Jun. 24, 1991, Pat. No. 5,344,832, which is a continuation-in-part of Ser. No. 463,327, Jan. 10, 1990, abandoned, which is a continuation-in-part of Ser. No. 192,332, May 10, 1988, abandoned.

[51] **Int. Cl.<sup>6</sup>** ..... **A61K 38/00**[52] **U.S. Cl.** ..... **514/12; 436/87; 436/811; 514/250; 514/288; 514/338; 514/866**[58] **Field of Search** ..... **436/71, 87, 811; 514/250, 288, 866, 338, 12**[56] **References Cited****U.S. PATENT DOCUMENTS**

4,219,555	8/1980	Rucman	424/250
4,239,763	12/1980	Milavec	424/261
4,659,715	4/1987	Meier	514/288
4,749,709	6/1988	Meier	514/288
4,783,469	11/1988	Meier	514/288
5,006,526	4/1991	Meier	514/288

**FOREIGN PATENT DOCUMENTS**

890369	9/1980	Japan
PCT/US92/05074	6/1992	WIPO
PCT/US92/11166	12/1992	WIPO

**OTHER PUBLICATIONS**

Iranhanesh et al. "Attenuated Pulsatile Release of Prolactin in Men with Insulin-Dependent Diabetes Mellitus" 1990 pp. 73-77.

Haisenleder et al. "The Effect of Dopamin Antagonists and/or VIP on TRH or VIP Induce Prolactin Release" 1988 pp. 341-349.

Marken et al. "Management of Psychotropic-induced Hyperprolactinemia" Oct. 1992 pp. 851-855.

Cassar, J. et al. "Bromocriptine Treatment of Acromegaly," *Metabolism* 26: 539-546 (1977).Doloecek, R. et al. "Bromocriptine and glucose tolerance in acromegals," *Pharmatherapeutica* 3: 100-106 (1982).Eskildsen, P. C. et al. "Long-Term Treatment of Acromegaly with Bromocriptine," *Acta Endocr.* 87: 687-700 (1978).Steinbeck, K. and J. R. Turtle, "Treatment of Acromegaly with Bromocriptine," *Aust. N. Z. J. Med.* 9: 217-224 (1979).

(List continued on next page.)

**Primary Examiner**—Donald E. Czaja**Assistant Examiner**—Lien Tran**Attorney, Agent, or Firm**—Darby & Darby, P.C.[57] **ABSTRACT**

Disclosed are methods for detecting abnormalities in prolactin daily rhythms. The methods involve comparing a prolactin profile of a vertebrate (including a human) subject being tested that has been compiled over a predetermined period to a predetermined standard prolactin profile for healthy subjects. The method also involves determining whether the vertebrate subject has an abnormal daily prolactin rhythm by ascertaining whether (i) at any point during waking hours the prolactin level of the subject being tested is greater than 1 SEM above the normal prolactin profile of said healthy subjects, and/or (ii) at any point during sleep-time the prolactin level of the subject being tested is at least 1 SEM lower than the normal prolactin profile of said healthy subjects. Also provided are methods for determining adjustments needed to an abnormal prolactin profile (or daily rhythm) to cause it to conform to the prolactin profile (or rhythm) of a healthy subject, and methods for effecting such adjustments.

**48 Claims, 5 Drawing Sheets**